

December 18, 1924.

Dr. Simon Flexner,
The Rockefeller Institute,
New York City, N.Y.

My dear Dr. Flexner:-

As a result of our conference last Saturday I thought that I would send you an outline of my general plan of work for next year.

We have found that bone-marrow can be depleted in the pigeon, rabbit and rat by procedures different from each species and in such a way that the marrow can be readily brought back to normal. In following the regeneration it appears that red blood-cells come back in an entirely different manner from the white cells.

1. The red blood-cells regenerate within collapsed capillaries in zones in which the sinuses which carry blood are markedly constricted, indicating zones of low oxygen tension. This correlates with observations made in high altitudes. Figure 1 is from a pigeon's marrow with a vascular injection with ink and shows very few patent sinuses but many collapsed capillaries in which reds are beginning to form. There are no white blood-cells in this area. Correlated with this condition of the marrow, the fat has disappeared and its place has been taken by a gelatinous substance. Gelatinous marrow has often been noted by pathologists. We correlate its appearance with a condition in which red cells are beginning to form. Hence we think that the formation of red blood-cells is correlated with low oxygen tension plus a gelatinous substance in the marrow. Our plan is to get the help of a chemist to extract the substance which makes the marrow gelatinous. We will furnish the gelatinous state. I do not know how much of the gelatinous substance a chemist would need so my estimates of animals for next year might vary within some what wide limits.

2. Figure 2 shows the condition of the marrow when white blood cells are forming. The vessels are practically all wide open sinuses, filled with circulating blood. We think that this means that substances for the white cells are brought in the blood stream. This correlates with the fact that we got such a marked maturation of the myeloblasts after transfusions in the case of leucemia we reported in the December number of the Journal of Experimental Medicine. Also, Carrel's growth producing substances in leucocytes, and the showers of dead leucocytes in the circulating blood of which I showed you the charts of Saturday, all indicate that we may find specific chemical substances from the white blood-cells themselves to experiment with on the origin of the white cells. This phase of the subject then also needs help from a chemist. In this work we should want to follow transfusions made in the hospital with vital studies on the blood-cells; also we should want to follow the blood of patients and animals getting radium or X-rays. But it seems to me that the fundamental attack must now be to find the chemical substances that influence the formation of red cells as distinct from the white cells. For the depletion of the rabbit's marrow we need inactivated cultures of bacilli, thus we need help from the bacteriological side. Dr. Doan, however, is fully competent to carry that end of the work.

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Dr. Doan is coming here Monday; and his letter sounds to me hopeful. I am very keen to get him. I think that he may have gotten started on a quite brilliant line of work all his own on the leucocytes which he could also carry on with us. I feel that he would be a very great addition to our group, but I do not think that Dr. Peabody will be very willing to let him go. I know that his salary this year is \$ and all his living expenses since he lives at the Boston City Hospital.

I spoke today to one of our fourth year men, a Mr. A. W. Cavins. He has a very fine record in the medical school. He did some chemical research with Dr. Shipley which was published in the Journal of Biological Chemistry, 1924, lix, 237. I am sending you a reprint. Under the advice of Dr. Amos he has applied for a medical internship here and from his record I should say that he will be practically certain to get it. He seemed very much attracted by the idea of the problem on leucemia but he may decide toward taking a general internship first. I think that he is a very able young man fully worth bringing into research for a permanent career. He will talk the matter over with Dr. Amos, whom he knows well and let me know this week whether he would seriously consider it; on Saturday he goes home to Indianapolis and it occurs to me that he might come back through New York to see you.

I have a Japanese, a Dr. Suguyama, sent here by the Japanese Government to prepare himself for a chair in Pathology in Japan. He chose of his own accord to come here and work in histology and embryology as a preparation. We have brought him into our group on the blood work. He has as his own problem the development of the white cells in the chick and is already getting some results. Then he joins us in the studies of the living blood cells in our experimental animals. He is really able; his plan is to stay here this year and perhaps go to Germany next year, but I think that he might be very attracted by the idea of going to the Institute next year. His expenses here are paid by the Japanese Government. I judge he has not a very large grant because he had to stay here all summer rather than go to a cooler place. With a small additional grant to cover the increased living expenses in New York, it occurs to me that he might be very glad to go on with the work next year. He took courses in Embryology at the University last spring.

During this fall a Hungarian, a Dr. George St. De Renyi, visited the laboratory. He had been a Rockefeller Fellow and had spent a year with Dr. Chambers at Cornell, in New York City. Our young Hungarian in the laboratory said that Dr. Renyi was quite the ablest young Anatomist in Hungary. Dr. Renyi made a great impression on all of us. He would be very glad to come to America but by the conditions of his Fellowship he must go back to Hungary to teach this coming year. He is worth our keeping in mind because he is a very competent man. I will find out from Dr. Doan if there is some one at Harvard and from Dr. Richards if we can get some one from Pennsylvania.

I will send to Mr. Smith a general estimate of equipment for next year within a few days and will let you know at once the result of my conference with Dr. Doan. He might also stop to see you on his way back to Boston after Christmas.